IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Denis P. Snider
Appl'n. No.	:	08/634,039
Filed	:	April 17, 1996
Title	:	METHODS AND COMPOSITIONS CONTAINING ANTIGENS HAVING A TARGETING MOIETY SPECIFIC FOR ANTIGEN PRESENTING CELLS FOR INTRANASAL IMMUNIZATION
Grp./A.U.	:	1644
Examiner	:	Gerald R. Ewoldt
Docket No.	:	1038-588 MIS:jb
Date	:	September 3, 2003

APPEAL BRIEF

BY COURIER

Mail Stop AF
Commissioner of Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
U.S.A.

Dear Sir:

1. Introduction

This Appeal Brief is submitted pursuant to applicant's appeal of the Final Rejection dated August 6, 2002. Three copies of this Appeal Brief are submitted. The enclosed cheque includes the prescribed fee for an appeal Brief.

2. Extension of Time

Petition is hereby made to provisions of 37 CFR 1.136(a) for an extension of five months of the period for submission of this Appeal Brief. The enclosed cheque includes the prescribed fee for the extension of time.

3. Real Party of Interest

The real party of interest is McMaster University by virtue of a deed of Assignment from the inventor recorded at Reel/frame 8272/0624.

4. Related Appeals and Interferences

There are no related appeals and interferences known to the appellant, appellant's legal representative, or assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in this pending appeal.

5. Status of Claims

This application was filed with claims 1 to 9. Claim 9 is cancelled by an Amendment filed simultaneously herewith. The claims appealed appears in the Appendix hereto.

6. Status of Amendments

An Amendment after Final Action is being submitted simultaneously herewith and has not yet been acted on.

7. Summary of Invention

The invention is concerned with a method of generating an immune response to an antigen in a host by intranasal administration to the host of an antigen coupled to a targeting moiety specific for unique structures of antigen-presenting cells.

8. Issues

The issues to be determined in this appear are:

1. Rejection of claims 1 to 9 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al and Hameleers et al.

2. Rejection of claims 1 to 9 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al and Hameleers et al and US Patent No. 4,228,795.

9. Grouping of Claims

Claims 1 to 8 stand or fall together. Claim 9 has been cancelled.

10. Argument

(a) Background to the Invention

Current theories of immunology suggest that, in order to provide a potent antibody response, an antigen must be seen by both B cells, which subsequently develop into the antibody producing cells, and also by helper T-cells, which provide growth and differentiation signals to the antigen specific B-cells. Helper T-cells recognize the antigen on the surface of antigen- presenting cells (APC) in association with Class II major histocompatibility complex (MHC) gene products.

There are significant advantages in using proteins and peptides and other antigens such as polysaccharides derived from proteins of infectious organisms as components in subunit vaccines. The search for such suitable subunits constitutes a very active area of both present and past research. Advances in techniques of recombinant DNA manipulations, antigen and protein purification, peptide synthesis and cellular immunology have greatly assisted in this endeavour. However, a problem in the use of such materials as vaccines has been the relatively poor *in-vivo* immunogenicity of most protein subunits, polysaccharides and peptides. Generally, the immune response to vaccine preparations is enhanced by the use of adjuvants. However, the only currently licensed adjuvants for use in humans are aluminum hydroxide and aluminum phosphate, collectively termed alum, which is limited in its effectiveness as a potent adjuvant. There is thus a need for new adjuvants with the desired efficacy and safety profiles.

Several adjuvants, such as Freund's Complete Adjuvant (FCA), syntex and QS21, have been used in animals. A novel way of engaging both the B and T cell components of an immune response has been described, which uses anti-class II monoclonal antibodies (mabs) coupled to antigens to target class II bearing antigen presenting cells (APC's). Experiments carried out *in-vivo* in rodents and rabbits using this technology, have demonstrated convincing proof of enhancement in immunogenicity of antigens, in the absence of conventional adjuvants. Other cell surface markers such as Surface Immunoglobulin (sIg), and MHC class I, have been used to achieve targeting to APC's.

(b) The Invention

As noted above, the invention is a method of generating an immune response to an antigen in a host, including a human host, by intranasal administration to the host of an antigen coupled, preferably by a heterobifunctional linking molecule, to a targeting moiety specific for surface structures of antigen-presenting cells, preferably a monoclonal antibody. As noted above, antigen coupled to targeting moieties have previously been used to generate an immune response to the antigen by parenteral administration to a host. However, there was no reason to believe that the antibody conjugate would bind specifically to the nasal passages or be taken up by the epithelium having regard to the structures of such epithelial surfaces.

(c) Rejection of claims 1 to 9 under 35 USC 103 over Estrada et al in view of McDermott et al and Hameleers et al

Estrada et al is concerned with a technique for immunization of the intestinal tract of mice using protein antigen bound to antibodies specific for murine MHC class II molecules. The specific conjugates, consisting of hen avidin (AV) or hen egg lysozyme (HEL) covalently conjugated to anti-MHC-II antibodies, are administered orally (p.o.) or by direct intraduodenal (i.d.) injection into the intestinal lumen of mice. Applicants invention is not concerned with oral or intraduodenal administration of the antigen-antibody conjugates, but rather effects administration intranasally.

The results which are described in Estrada et al (page 904, right hand column) refer to obtaining a weak and inconsistent production of intestinal IgA-antibody. The results also recite that serum IgG and IgA response may be opitmized by high doses of antigen. Further, a significant mouse-to mouse variation in antibody response was apparent within any immunization group, leading to a study of direct injection into the duodenum.

The last paragraph of the article (p. 906, right hand column) alludes to further studies but there is no subsequent paper by this group relating to any further experiments. It must be construed from this fact that the mucosal administration procedure described in Estrada et al was not sufficiently promising to merit further work and the approach simply was abandoned.

It is submitted that, having regard to the work described in Estrada et al, a person skilled in the art would have no reason to believe that the antigen-antibody conjugate would bind specifically to the epithelium of nasal passages or be taken up by the epithelium.

The antibodies used in applicants experimentation have speciality for class II MHC molecules expressed by antigen presenting cells. These class II molecules are only poorly expressed by non-inflamed nasal epithetial cells in young rodents, as described in the Hameleers et al reference, Cell and Tissue Res. 256, p431-438 (1989), of record herein, and different from the Hameleers reference relied on by the Examiner. In addition, there is no evidence that MHC class II molecules are expressed on the external membrane (apical surface) of rodent nasal epithelical cells. Available immunohistochemistry suggests only intracellular localization of class II MHC in the rodent nasal epithelium and those published results cannot define apical expression, as described in the Koornstra et al, Acta Otolaryngol., 113, 660-667 (1993), of record herein.

With respect to these literature references, the Examiner stated in the Final Action of April 2, 2001 that:

> ".... the references were never submitted with any reply by Applicant nor were the references ever made of record in an IDS or on a Form PTO-892."

The applicants had submitted copies of those references and some additional references with a response filed June 5, 2000 along with a PTO-1449 listing the references. The next communication from the Office, the Office Action of August 22, 2000, appended the PTO-1449, initialled by the Examiner as having been considered. A copy of that document is enclosed for convenience.

Accordingly, it is submitted that it is unobvious that monoclonal antibody-antigen conjugates applied to the epithelical surfaces of the nasal passages would be able to reach circulation or even the underlying lymphoid tissue of the epithelium in substantial quantity and produce an immune response to the antigen. The applicant has demonstrated the provision of such an immune response. A person skilled in the art would understand that the epithetial layers of the nasal passages have tight junctions and that large molecules, such as antibodies and conjugates, do not pass through the epithelium, except with only poor efficiency.

Having regard to the work described by Estrada et al, discussed above, and the knowledge of the art, it is submitted that applicants results are surprising.

It is submitted that the secondary references do not remedy the defects of Estrada et al. McDermott et al is a discussion of immunity in the respiratory tract, which possesses lymphoid aggregates similar to the Peyer's patches of the intestinal tract.

Hameleers et al describes that nasal administration of thymus-dependent keyhole limpet haemocyanin (KLH) induced production of IgA and IgG antibodies to the trinitrophenylated (TNP) antigens. The immunogen was administered in the form of liquid droplets.

It is submitted that there is no motivation provided by the results reported in Estrada et al for any expectation of success in achieving an immune response utilizing immunotargeting by intranasal administration of an antigen coupled to a targeting moiety specific for surface structures of antigen-presenting cells.

In the Final Action, the Examiner gives the reason for rejection is:

> "... for the reasons of record as set forth in Paper No. 28, mailed 5/24/02"

Paper No. 28 is dated April 27, 2001 and it is assumed the Examiner is in error.

The Examiner expressed the view in the Final Action of April 27, 2001, that:

> "It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to immunize a subject according to the manner of Hameleers et al substituting the KLH carrier with an anti-MHC class II antibody as taught by Estrada et al. One would have been motivated to make the substitution with a reasonable expectation of success based upon the teachings of McDermott et al that the BALT of the respiratory tract is functionally similar to the PP of the intestines and the teachings of Estrada et al that the antibody conjugates specifically taught the antigen presenting cells in the intestine."

The BALT to which McDermott et al refers is not located in the nasal passages and hence there is no motivation provided. Applicants claims are specifically directed to intranasal administration to the epithelical surfaces in the nasal passages.

Having regard to the above, it is submitted that the Examiner is in error in rejecting claims 1 to 9 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al and Hameleers et al.

(d) Rejection of claims 1 to 9 under 35 USC 103 over Estrada et al in view of McDermott et al and Hameleers et al and US Patent No. 4,228,795

It is submitted that this rejection is moot in view of deletion of claim 9.

11. Summary

In summary, it is submitted that the rejection of claims 1 to 8 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al and Hameleers et al, should be REVERSED.

Respectfully submitted,

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APPENDIX

CLAIMS APPEALED

1. A method of generating an immune response to an antigen in a host, which comprises:

intranasally administering to said host an antigen coupled to a targeting moiety specific for surface structures of antigen-presenting cells.

2. The method of claim 1 wherein said antigen-presenting cells are selected from the group consisting of class I or class II major histocompatibility expressing cells (MHC), B-cells, T-cells, professional antigen-presenting cells including dendritic cells, and $CD4^+$ cells.

3. The method of claim 2 wherein the targeting moiety is a monoclonal antibody or a fragment thereof.

4. The method of claim 3 wherein the antigen is a protein, peptide, carbohydrate or ligand.

5. The method of claim 4 wherein the antigen is derived from a pathogen and said immune response is a protective immune response against disease caused by said pathogen.

6. The method of claim 5 wherein the immune response is an IgG or an IgA immune response.

7. The method of claim 5 wherein the host is a human host.

8. The method of claim 1 wherein said antigen is coupled to said targeting moiety through a heterobifunctional linking molecule.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

AIR MAIL

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/634,039	Applicant(s) Snider et al
	Examiner F. Pierre VanderVegt	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Jun 6, 2000* .

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-9* ~~is~~/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9* ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *22*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

Claims 1-9 are currently pending in this application.

Continued Prosecution Application

1. The request filed on June 6, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/634,039 is acceptable and a CPA has been established. An action on the CPA follows.

2. In view of the amendment filed June 6, 2000, no outstanding rejections are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Estrada et al (38 on form PTO-1449) in view of McDermott et al (10) and Hamaleers et al (15).

The Estrada et al reference teaches immunization of subjects via the intestinal mucosa using antigen covalently conjugated to anti-MHC Class II antibodies (see entire document). Estrada et al further teaches that these conjugates effectively induce production of IgA and IgG antibodies in mice (Abstract in particular). Estrada et al also teaches that conjugation was effected via the hetero-bifunctional cross-linker SMPB (page 902, first column in particular). Estrada et al does not teach intranasal administration. McDermott et al teaches that the respiratory tract possesses lymphoid aggregates similar to the Peyer's patches (PP) of the intestinal wall (paragraph bridging pages 57 and 58 in particular) termed BALT and that the lymphoepithelium of BALT resembles that of the PP (last paragraph of page 59 in particular). McDermott et al further teaches that BALT is exposed to inhaled antigens because of its location

(last paragraph of page 63 in particular). McDermott et al further teaches that the gut can be viewed as a model for the lung and that studies of oral immunization can provide insight into respiratory tract immunization (page 93, section D in particular). Hamaleers et al teaches that nasal administration of trinitrophenylated (TNP) keyhole limpet hemocyanin (KLH) induced the production of IgA and IgG antibodies to TNP. KLH is commonly used in the art as a carrier for immunogenic haptens, as it is a classical stimulator of helper T cells through classical pathways. Hamaleers et al teaches the administration of the immunogen as liquid drops. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to immunize a subject according to the manner of Hamaleers et al substituting the KLH carrier with an anti-MHC Class II antibody as taught by Estrada et al. One would have been motivated to make the substitution with a reasonable expectation of success based upon the teachings by McDermott et al that the BALT of the respiratory tract is functionally similar to the PP of the intestines and the teachings of Estrada et al that the antibody conjugates specifically targeted the antigen presenting cells in the intestine. One would have been further motivated by the teachings of McDermott et al that local humoral immunity plays an important role in respiratory tract defense against airborne pathogens.

4. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Estrada et al (38 on form PTO-1449) in view of McDermott et al (10), Hamaleers et al (15) and Babington, U.S. Patent 4,228,795 (C on form PTO-892).

Estrada et al, McDermott et al and Hamaleers et al have been discussed supra. The combination of references does not teach a disperser for dispersing an aerosol. Hamaleers et al further teaches that a large proportion of aerosolized antigens wind up in the intestines (page 119 in particular). McDermott et al teaches that this is due to swallowing and results in presentation to the immunological apparatus of the intestines (page 48 in particular). The '795 patent teaches a nebulizer which can be used to aerosolize medicants for nasal inhalation (Figure 4 and column 6, line 7 through column 8, line 54 in particular). The '795 patent further teaches that said nebulizer is suitable for use with viscous or sticky substances (column 8, lines 34-37 in particular). It would

have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the nebulizer taught by the '795 patent to administer the mAb-pathogenic antigen conjugate taught by Estrada et al to the nasal mucosa as taught by Hamaleers et al. One would have been motivated, with a reasonable expectation of success to combine these teachings by the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms and by the teachings of the '795 patent that the nebulizer is usable with sticky substances, which a common property of proteinaceous solutions. Further motivation for using the nebulizer of the '795 patent is provided by the knowledge that some individuals do not tolerate nose drops well.

Conclusion

5. References 1-50 on Applicant's form PTO-1449 filed June 6, 2000 have been lined through as duplicates of references previously cited as references 1-50 on Applicant's form PTO-1449 filed September 16, 1996, which were properly marked as having been considered.

6. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2000 366-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
August 18, 2000

F. PIERRE VANDERVEGT
PATENT EXAMINER

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT	ATTY. DOCKET NO. 1038-588 MIS:lm	SERIAL NO. 08/634,039
	APPLICANT Denis P. Snider et al.	
	FILING DATE June 7, 1996	GROUP 1644

U.S. PATENT DOCUMENTS

*INITIAL		DOCUMENT NO.	DATE	NAME	CLASS	SUBCL.	FILING DATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCL.	TRANSLATION	
							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		(1)	Warren, H.S.; Vogel, F.R. and Chedid, L.A.A.; Ann. Rev. Immun. (1986) **4**:369-388.
		(2)	Carayanniotis, G. and Barber, B.H.; Nature (Lond.) (1987) 327:59-61.
		(3)	Carayanniotis, G.; Vizi, E.; Parker, J.M.R.; Hodger, R.S. and Barber, B.H.; Mol. Immunol. (1988) **25**:907-911.
		(4)	Skea, D.L.; Douglas, A.R.; Skehel, J.J. and Barber, B.H.; Vaccine (1993) **11**:994-999.
		(5)	Carayanniotis, G.; Skea, D.L.; Luscher, M.A. and Barber, B.H.; Mol. Immunol. (1991) **28**:261-267.
		(6)	Kawamura, H. and Berrofsky, J.A.; J. Immunol. (1986) **136**:58-65.
		(7)	Casten, L.A.; Kawmaya, P. and Pierce, S.K.; J. Exp. Med. (1988) **168**:171-180.
		(8)	Casten, L.A. and Pierce, S.K.; J. Immunol. (1988) **140**:404-410.
		(9)	Kilian, M. and Russell, M.W.; Handbook of Mucosal Immunology (Eds. Ogra, P.L.; Mesteck, J.; Lamm, M.E.; Strober, W.; McGhee, J.R.; and Bienenstock, J.;) Academic Press, San Diego, (1994) 127-140.
		(10)	McDermott, M.R.; Befus, A.D. and Bienenstock, J.; Int. Rev. Exp. Pathol. (1982) **23**:47-112.
		(11)	Tamura, S.; Kurata, H.; Fumato, H.; Nagamine, T.; Aizawa, C. and Kurata, T.; Vaccine (1989) **7**:314-320.
		(12)	Nedrud, J.G.; Liang, X.; Hague, N. and Lamm, M.E.; J. Immunol. (1987) **139**:3484-3492.
		(13)	Wu, H.Y. and Russell, M.W.; Infect. Immun. (1993) **61**:314-322.
		(14)	Bessen, D. and Fischetti, V.A.; J. Immunol. (1990) **145**:1251-1256.
		(15)	Hameleers, D.M.H.; van der Ven, I.; Bievenga, J. and Sminia, T.; Immunol. Cell Biol. (1991) **69**:119-125.
		(16)	Aramaki, Y.; Fujii, Y.; Kikuchi, H. and Tsuchiya, S.; Vaccine (1994) **12**:1241-1245.
		(17)	Wu, H.-Y. and Russell, M.W.; Vaccine (1994) 12:215-222.
		(18)	Langermann, S.; Palaszynski, S.; Sadziene, A.; Stover, C.K. and Koenig, S.; Nature (1994) 372:552-555.
		(19)	Cahill, E.S.; O'Hagan, D.T.; Illum, L.; Barnard, A.; Mills, K.H.G. and Redhead, K.; Vaccine (1995) **13**:455-462.
		(20)	Tamura, S.I.; Samegai, Y.; Kurata, H.; Kikuta, K.; Nagamine, T.; Aizawa, C. and Kurata, T.; Vaccine (1989) **7**:257-262.
		(21)	Reuman, P.D.; Keely, S.P. and Schiff, G.M.; J. Med. Virol. (1991) **35**:192-197.
		(22)	Tamura, S.; Yamanaka, A.; Shimohara, M.; Tomita, T.; Komase, K.; Tsuda, Y.; Suzuki, Y.; Nagamine, T.; Kawahara, K.; Danbara, H.; Aizawa, C.; Oya, A. et al; Vaccine (1994) **12**:419-426.

EXAMINER	DATE CONSIDERED

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY DOCKET NO. 1038-588 MIS:lm	SERIAL NO. 08/634,039
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							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		(23)	Hirabayashi, Y.; Kurata, H.; Funato, H.; Nagamine, T.; Aizawa, C.; Tamura, S.; Shimada, K. and Kurata, T.; Vaccine (1990) **8**:243-248.
		(24)	Loevgren, K., Kaberg, H. and Morein, B. Clin Exp. Immunol. (1990) 82:435-439
		(25)	Oka, T.; Hayde, T.; Maeshima, K.; Gonaga, A.; Ohkuma, K. and Sakob, M.; Vaccine (1994) 12:1255-1258
		(26)	Lipscombe, M.; Charles, I.G.; Roberts, M.; Dougan, G.; Tite, J. and Fairweather, N.F.; Mol. Microbiol. (1991) 5:1385-1392.
		(27)	Hajishengallis, G.; Hollingshead, S.K.; Koga, T. and Russell, M.W.; J. Immunol. (1995) **154**:4322-4332.
		(28)	De Haan, A.; Geerligs, H.J.; Huchshorn, J.P.; Van Scharrenburg, G.J.M.; Palache, A.M. and Wilschut, J.; Vaccine (1995) **13**:155-182.
		(29)	van Heyningen, S.; Science (1974) **183**:656-657.
		(30)	Mestecky, J.; J. Clin. Immunol. (1987) **7**:265-276.
		(31)	Croitoru, K.; Bienenstock, J.; Handbook of Mucosal Immunology, San Diego, CA: Academic Press, Inc. (1994) 141-149.
		(32)	Bienenstock, J.; Johnston, N.; Perey, D.Y.; Lab. Invest. (1973) **28**:686-692.
		(33)	Bienenstock, J.; Johnston, N.; Perey, D.Y.; Lab. Invest. (1973) **28**:693-698.
		(34)	Pabst R.; Immunology Today (1992) **13**:119-122.
		(35)	Kuper, C.F., Koornstra, P.J.; Hameleers, D.M.H.; Biewenga, J.; Spit, B.J.; Duijvestijn, A.M.; van Breda Vriesman, P.J.C., and Sminia, T. Immunol. Today (1992) **13**:219-224.
		(36)	Elson, C.O. and Ealding, W.; J. Immunol. (1984) **132**:2736-2742.
		(37)	Lycke, N. and Holmgren, J. Immunology (1986) **59**:301-307.
		(38)	Estrada, A.; McDermott, M.R.; Underdown, B.J. and Snider, D.P.; Vaccine (1995) **13**:901-907.
		(39)	Mjaaland, S. and Fossum, S.; Int. Immunol. (1991) **3**:1315-1321.
		(40)	Heukeshoven, J. and Dernick, R.; Electrophoresis (1988) 28-32.
		(41)	Snider, D.P.; Marshall, J.S.; Perde, M.H. and Liang, H.; J. Immunol. (1994) **153**: 647-657.
		(42)	Graham, M.B.; Dalton, D.K.; Giltinan, D.; Braciale, V.L.; Steward, T.A. and Braciale, T.J.; J. Exp. Med. (1993) **178**:1725-1732.
		(43)	Fazekas, G.; Rosenwirth, B.; Dukor, P.; Gergely, J.; and Rjnavolgyi, E.; Eur. J. Immunol. (1994) **24**:3063-3067.
		(44)	Iwasaki, T. and Nozima, T.; J. of Immunol. (1997) **118**:256-263.

EXAMINER	DATE CONSIDERED

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT	ATTY. DOCKET NO. 1038-588.[illegible]	SERIAL NO. 08/634,039
	APPLICANT Denis P. Snider et al	
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U.S. PATENT DOCUMENTS

*INITIAL		DOCUMENT NO.	DATE	NAME	CLASS	SUBCL	FILING DATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCL	TRANSLATION	
							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

(45) Fujihashi, K.; Yamamoto, M.; McGhee, J.R. and Kiyono, H.; J. Immunol. (1993) **151**:6681-6691.

(46) Kuper, C.F.; Koornstra, P.J. Hameleers, D.M.H.; Biewenga, J.; Spit, B.J.; Duijvestijn, A.M.; Van Breda Vriesman, P.J.C. and Sminia, T. Immunol. Today (1992) **13**:219-224.

(47) Spit, B.J.; Hendriksen, E.G.J.; Bruijntjes, J.P. and Kuper, C.F.; Cell Tissue Res. (1989) **255**:193-198.

(48) Owen, R.L.; J. Exp. Med. (1994) **180**:7-9.

(49) Neutra, M.R. and Kraehenbuhl, J.-P.; Trends Cell Biol. (1992) **2**:134-137.

(50) Weltzin, R.; Lucia-Jandris, P.; Michetti, P.; Fields, B.N.; Kraehenbuhl, J.P. and Neutra, M.R.; J. Cell Biol. (1989) **108**:1673-1685.

EXAMINER	DATE CONSIDERED

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT	ATTY. DOCKET NO. 1038-588 MIS:ja	SERIAL NO. 08/634,039
	APPLICANT Denis P. Snider	
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U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCL.	TRANSLATION	
							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

R		51. Fossum, S. et al, Semin. Immunol. 4, 275-283 (1992).
		52. Tamura, et al, Microbiol. Immunol. 32, 1145-1161 (1988)
		53. Lycke et al, Scand. J. Immunol. 33, 691-698 (1991).
		54. Hameleers et al, Cell Tissue Res. 256, 431-438 (2000).
		55. Koornstra et al. Acta Otolaryngol. 113, 660-667 (1993).
		56. Snider et al. Immuno. 90, 323-329 (1997).
		57. Wu et al, Infect. Immun, 61, 314-322 (1993).
		58. King et al. J. Infect, Diseases 127, 639-647 (1973).
		59. Middlebrook et al, Microbiol. Rev. 48, 199-221 (1984).
		60. Spangler, B.G., Microbial Rev, 56, 622-647 (1992).
		61. Snider, D.P., Crit. Rev. Immunol., 15, 317-348 (1995)
		62. Holgren et al, Immunol. Comm., 5, 737-756 (1976).

EXAMINER: D. [signature] DATE CONSIDERED: 8/17/2000

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if in conformance and not considered. Include copy of this form with next communication with applicant.

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